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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/618,493	07/11/2003	Luz Montesclaros	5063 US	5407

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EXAMINER	
SCHNIZER, RICHARD A	
ART UNIT	PAPER NUMBER
1635	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/618,493	MONTESCLAROS ET AL.	
	Examiner	Art Unit	
	Richard Schnizer, Ph. D.	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-18,20,21 and 23-33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-18, 20, 21, and 23-33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/30/06 has been entered.

Claim 22 was canceled in the amendment filed 11/30/06.

Claims 1-18, 20, 21, and 23-33 remain pending and are under consideration in this Office Action.

Request for Interview

At page 17 of the response filed 11/30/06, Applicant set forth a request for an interview in the event that the application was not found to be in condition for allowance. This request was attached to an amendment which must be acted on by the Office in a timely fashion. In the future, Applicant is invited to contact the Examiner directly to arrange any interviews prior to the submission of amendments, so that any remaining issues can be discussed in a timely fashion.

Claim Rejections/Objections Withdrawn

Applicants amendments were sufficient to overcome the rejection of claims 14-17 under 35 USC 102 over Domanico.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8, 14-18, 20, 21, and 23-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuipers et al (Ann. Rheum. Dis. 58: 103-108, 1999) in view of Domanico et al (US Published Application 20040180445).

Kuipers taught a method of isolating Chlamydia genomic DNA by treatment of synovial fluid with proteinase K and a nonionic detergent, addition of this mixture to a solid support, and elution of DNA from the support. See abstract; Fig. 1 on page 104, method 4a; see also page 104 last paragraph to page 105, second full paragraph of column 1.

Kuipers taught a method of isolating Chlamydia genomic DNA by treatment of synovial fluid with proteinase K and either an ionic or a nonionic detergent, addition of the cationic lipid CTAB, addition of a solid support, and elution of the DNA from the support. See abstract; Fig. 1 on page 104, e.g. methods 3b, 3c, 4b, and 4c; see also

second and third full paragraphs of column 2 on page 104; and first two full paragraphs on page 105.

Kuipers did not teach a zwitterionic detergent or a chaotrope, and does not disclose wash solutions.

Domanico taught compositions for gently lysing and solubilizing a host cell comprising: a buffering agent, a zwitterionic detergent, and a chaotropic salt. See abstract and claim 8. Domanico also stated that the compositions could be used for preferential isolation of high molecular weight nucleic acids. See paragraph 13 at page 2. Host cells include mammalian cells, see paragraph 30 on page 2. Zwitterionic detergents taught by Domanico include n-Tetradecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate, n-Octyl-N,N-dimethyl-3-ammonio-1-propanesulfonate, n-Dodecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate, Anzergent 3-14, Analytical Grade; Anzergent 3-8, Analytical Grade; Anzergent 3-10, Analytical Grade; Anzergent 3-12, Analytical Grade, respectively or zwittergent 3-8, zwittergent 3-10, zwittergent 3-12 and zwittergent 3-14, CHAPS, CHAPSO, Apo10 and Apo12. See paragraph 53 on page 5. Disclosed chaotropic agents include guanidine hydrochloride, guanidine thiocyanate, urea and sodium iodide. It is also clear from the teachings of Domanico that non-ionic and zwitterionic detergents could be used as alternatives to lyse cells in DNA isolation procedures. See e.g. paragraph 9 on page 1. Domanico also exemplified the use of two chaotropes together in a single lysis buffer.

Domanico also taught wash solutions comprising Tris buffer salts and alcohols, and alkaline elution buffers, for use with DNA-binding silica matrices. See e.g. abstract; paragraphs 36, 72, and 73.

It would have been obvious to one of ordinary skill in the art at the time of the invention to substitute a zwitterionic detergent for the nonionic detergent in the method of Kuipers because Domanico taught that non-ionic and zwitterionic detergents could be used as alternatives to lyse cells in DNA isolation procedures. See e.g. paragraph 9 on page 1. In fact, Domanico taught that the choice of detergents was a result-effective variable and explored the use of various different detergents and detergent mixtures, including a mixture of an ionic and a non-ionic detergent (see e.g. paragraphs 99 and 109 on page 9, and Table 5 on page 10. In view of the fact that use of non-ionic, anionic, cationic, and zwitterionic detergents in combination was known in the art at the time of the invention, and the fact that it was recognized that the identity of the detergents used influenced results, it would have been obvious to one of ordinary skill in the art at the time of the invention to optimize the detergent content of a nucleic acid isolation mixture in order to maximize nucleic acid yield and purity. Similarly, it was well known in the art at the time of the invention that chaotropic compounds were useful in the isolation of nucleic acids from cells, e.g. Domanico taught that chaotropic salts were useful in nucleic acid isolation procedures to drive the binding of nucleic acid to a solid support matrix (see paragraph 44), and taught the use of two chaotropes together in a single lysis buffer. Accordingly, it would have been obvious to one of ordinary skill in

the art to use the chaotropes of Domanico in the method of Kuipers to aid in the binding of the DNA to the solid support.

Pertinent to claims 21 and 23-31, it would have been obvious to one of ordinary skill in the art at the time of the invention to organize into a kit the elements of the invention of Kuipers as modified by Domanico because one of ordinary skill in the art appreciates that organizing experimental reagents prior to use is standard laboratory practice which reduces the frequency of errors. Moreover, because Kuipers used a solid silica support to bind DNA, it would have been obvious to use the wash solutions of Domanico that are designed for washing and eluting DNA from silica supports. See e.g. paragraph 36.

Claims 9-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuipers et al (Ann. Rheum. Dis. 58: 103-108, 1999) and Domanico et al (US Published Application 20040180445) as applied to claims 1-8, 14-18, 20, 21, and 23-31 above, and further in view of Gautsch et al (US Patent 6,235,501).

The teachings of Kuipers (1999) and Domanico are discussed above and can be combined to render obvious a method of isolating Chlamydia genomic DNA from synovial fluid using a protease, a zwitterionic detergent, a chaotropic agent, and a solid support.

While Kuipers taught the use of the cationic detergent CTAB in methods of genomic DNA isolation in conjunction with the use of a solid phase (see Fig. 1 on page 104, especially methods 4b and 4c), these methods require organic extraction prior to

application of the DNA to the solid phase. This extraction would likely remove at least the protease from the lysate, such that the combination applied to the solid phase would not comprise a protease. For this reason, the combined references did not teach application of the claimed combination to the solid phase.

Gautsch taught the use of CTAB in lysis methods wherein the lysate is subsequently applied to a solid phase for binding and purification of DNA, (see e.g. claims 24 and 37) but Gautsch did not teach any organic extraction of the CTAB-containing lysate prior to application to the solid phase. It follows that one of ordinary skill in the art at the time of the invention would realize that the organic extraction step lysates comprising CTAB can be applied directly to a solid phase for DNA purification such that the organic extraction steps of Kuipers methods 4b and 4c are not required, and can be omitted. One would be motivated to omit the extraction step in order to save time and reagents. It would have been similarly obvious to modify the method of Kuipers by adding a zwitterionic detergent and one or more chaotropes for the reasons set forth in the previous rejection. The resulting mixture would comprise the protease, the zwitterion, the chaotrope(s) and CTAB at the time it was applied to the solid phase. Thus the invention as a whole was prima facie obvious.

Claims 32 and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kuipers et al (Ann. Rheum. Dis. 58: 103-108, 1999) and Domanico et al (US Published Application 20040180445) as applied to claims 1-8, 14-18, 20, 21, and 23-31

above, and further in view of Kuipers et al (Arthritis and Rheumatism, (1998 Oct) Vol. 41, No. 10, pp. 1894-5).

The teachings of Kuipers (1999) and Domanico are discussed above and can be combined to render obvious a method of isolating Chlamydia genomic DNA from synovial fluid using a protease, a zwitterionic detergent, a chaotropic agent, and a solid support.

These references did not teach isolation of nucleic acids from blood.

Kuipers (1998) taught a method of detecting Chlamydia genomic DNA from peripheral blood leukocytes.

It would have been obvious to one of ordinary skill in the art at the time of the invention to apply the DNA isolation procedure of Kuipers as modified by Domanico to blood or to any other tissue with a reasonable expectation of success Domanico taught that the combination of a zwitterionic detergent and chaotropic agent could be used to lyse a wide variety of cells including mammalian cells, insect cells, and bacterial cells. There is no reason to doubt that the method could be used to isolate DNA from blood cells.

Response to Arguments

Applicant's arguments filed 11/30/06 have been fully considered as they apply to the grounds of rejection set forth above but they are not persuasive.

Applicant addresses the rejection over Kuipers in view of Domanico at pages 13-15 of the response. Applicant correctly argues that the methods disclosed in Kuipers

that were cited in the previous (i.e. methods 3b, 3c, 4b, and 4c) would not result in the application to the solid phase of a combination comprising at least one protease and at least one zwitterionic agent. However, the grounds of rejection set forth above clarify that the method 4a of Kuipers, when combined with Domanico will result in application of the claimed combination to the solid phase. Further the rejection citing Gautsch makes clear that one of ordinary skill in the art would have been motivated to omit the organic extraction step from Kuipers methods 4b and 4c, such that these methods, as modified in view of Domanico, would also result in application of the claimed combination to the solid phase. Regarding claims 21 and 25-31, Applicant repeats the arguments addressed above, and further states that the Examiner as not provided any evidence that one of ordinary skill would have been motivated to assemble the claimed kits. Applicant's argument is unpersuasive because one of ordinary skill in the art appreciates that organizing experimental reagents prior to use is standard laboratory practice which reduces the frequency of errors. Applicant has not provided any reason or logic to indicate that this is not so. MPEP 2144.02 indicates that the rationale to support a rejection under 35 USC 103 may rely on logic and sound scientific principle. The fact that the organizing of reagents leads to fewer errors is considered to be a logic scientific principle that is apparent to those of ordinary skill.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11

F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-3, 5-12, 14,15, 17, 18, 21 and 23-30 stand rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-64 of U.S. Patent No. 6,762,027. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

The claims of '027 are drawn to methods and kits for methods and kits for contacting whole tissue with a disrupting buffer comprising a protease and a cationic surfactant, substantially neutralizing the surfactant, and binding the nucleic acid to a solid phase. The specification teaches at column 10, lines 8-18 that "substantially neutralizing" embraces addition of one or more of chaotropes, nonionic surfactants, anionic surfactants, and zwitterionic surfactants. So, it would have been obvious through routine optimization to assess the activity of various combinations of chaotropes, nonionic surfactants, anionic surfactants, and zwitterionic surfactants, such as those required in instant claims 5-7, 11, 12, and 15. Claim 5 of '027 requires the use of the cationic surfactants of instant claims 10, 12, and 13. Claim 7 of '027 requires the use of a chaotrope selected from the group: NaBr, NaI, NaSCN, LiCl, LiBr, LiI, GuHCl, and GuSCN. Claim 25 of '027 requires isolating the bound nucleic acid, i.e. eluting it

from the solid support. It is clear from the specification as a whole the claimed methods result in isolating genomic DNAs, see e.g. the brief descriptions of Figs. 13-30, at columns 3 and 4. Claim 15 of '027 requires the use of proteinases selected from proteinase K, proteinase, R, proteinase T, subtilisin DY, an alkaline serine protease from Streptomyces griseus, an alkaline serine protease from Bacillus lichenformis, dispase, subtilisin Calsberg, subtilopeptidase A, and thermolysin.

'027 does not teach a kit with wash or elution solutions, however, claims 25-40 require elution of the nucleic acid from the solid support. The portion of the specification supporting these claims teaches that solid supports comprising DNA were washed in 90% ethanol and DNA was eluted in an alkaline solution buffered with Tris HCl and with a second solution of NaOH. See column 36. lines 31-41. It would have been obvious to one of ordinary skill in the art at the time of the invention to add the wash and elution solutions to the kits of the '027 patent simply because these solutions allow isolation of nucleic acids purified by the methods claimed in the '027 patent.

Claims 4, 13, 16, 20, and 31 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-64 of U.S. Patent No. 6,762,027 as applied to claims 1-3, 5-12, 14,15, 17-19, and 21-30 above, and further in view of Domanico et al (US Published Application 20040180445). Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons.

The teachings of the '027 patent are discussed above. Although '027 teaches zwitterionic surfactants, it does not exemplify any.

Domanico taught a method of isolating nucleic acids from bacterial, insect or mammalian cells by treating the cells with a lysis solution comprising guanidine hydrochloride, guanidine thiocyanate, and the zwitterionic detergent N-decyl-N,N-dimethyl-3-ammonio-1-propanesulfonate, and binding the nucleic acid to a solid matrix such as glass beads. See e.g. abstract, paragraph 30 on page 2, Table 3 at page 8, and e.g. paragraphs 99-109 on page 9. Other zwitterionic detergents taught by Domanico include n-Tetradecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate, n-Octyl-N,N-dimethyl-3-ammonio-1-propanesulfonate, n-Dodecyl-N,N-dimethyl-3-ammonio-1-propanesulfonate, Anzergent 3-14, Analytical Grade; Anzergent 3-8, Analytical Grade; Anzergent 3-10, Analytical Grade; Anzergent 3-12, Analytical Grade, respectively or zwittergent 3-8, zwittergent 3-10, zwittergent 3-12 and zwittergent 3-14, CHAPS, CHAPSO, Apo10 and Apo12. See paragraph 53 on page 5.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the zwitterionic detergents of Domanico in the methods and kits of '027 because the claims of '027 require substantial neutralization of a cationic surfactant, and the specification of '027 teaches at column 10, lines 8-18 that "substantially neutralizing" embraces addition of one or more of chaotropes, nonionic surfactants, anionic surfactants, and zwitterionic surfactants. The zwitterionic surfactants of Domanico are used in a similar method, so it would have been clear to one of ordinary skill in the art at the time of the invention to use them in the methods and kits of the '027

patent. Regarding the tissue sources of instant claim 20, the "tissue" of the '027 claims includes biopsy materials and aspirates; in vitro cultured cells, including primary and secondary cells, transformed cell lines, and tissue and cellular explants; lymph; and body fluids such as urine, sputum, semen, secretions, eye washes and aspirates, lung washes and aspirates.

Response to Arguments

Applicant's request to hold the rejection in abeyance until allowable subject matter is identified, filed 11/30/06, is noted.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 571-272-0762. The examiner can normally be reached Monday through Friday between the hours of 6:00 AM and 3:30. The examiner is off on alternate Fridays, but is sometimes in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, J. Douglas Schultz, can be reached at (571) 272-0763. The official central fax number is 571-273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

(Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

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